

### Remarks

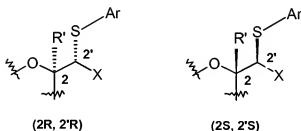
Claims 1-5 and 10-15 are currently pending. Claims 10-14 have been cancelled. New claim 16 has been added, claiming the use of the compounds of Formula I for the treatment of persistent pain. Applicants assert that new claim 16 raises no issue of new matter. Basis for new claim 16 may be found on page 8, lines 24-25 and page 9, line 27 in the specification. Entry of the amendments and allowance of the claims in view of the amendments and following discussion are respectfully requested.

### Rejection Under 35 USC § 112

The Examiner rejected claims 10-14 under 35 USC § 112, first paragraph allegedly for lack of enablement. The Examiner stated that the specification was enabling for the treatment of persistent pain. In view of the rejection and the Examiner's statement, Applicants have cancelled claims 10-14 and added new claim 16, which is limited to a method of treating persistent pain. Withdrawal of this rejection in view of the amendment and allowance of new claim 16 is respectfully requested.

### Provisional Rejection Under Non-Statutory Double Patenting

Claims 1-5 and 10-15 stand provisionally rejected as being unpatentable in view of claims 1-7, 14, 15 and 18 of co-pending application 10/524,650. The Examiner has accurately characterized the stereochemical relationship between the compounds claimed in the present application (2R, 2R') and in the co-pending application (2S, 2S') as illustrated below:



Applicants assert, however, that the skilled artisan would not expect that this structural modification would give rise to the observed significant differences in pharmacological properties.

All of the exemplified (2R, 2R') compounds claimed in the present application are taught to potently inhibit both the norepinephrine and serotonin transporters, exhibiting a  $K_i < 100$  nM at each transporter (specification, page 64, lines 14-15). The exemplified (2S, 2S') compounds claimed in co-pending application 10/524,650 are taught to inhibit the norepinephrine transporter, exhibiting a  $K_i < 500$  nM (10/524,650, page 56, line 22). These (2S, 2S') compounds are also taught to be selective for the norepinephrine transporter relative both the serotonin and dopamine

transporters by a factor of at least 5 (10/524,650, page 56, lines 23-26). Modifying only the stereochemistry of the (2S, 2S') compounds claimed in 10/524,650 to provide the (2R, 2R') compounds or the present application introduces potent serotonin transporter inhibitory activity. Applicants are not aware, and the Examiner has not identified, any reference that would teach or suggest that the skilled artisan would expect that a change in stereochemistry would give rise to this new pharmacological effect. As such, Applicants assert that the provisional double-patenting rejection in the present application is improper. Withdrawal of this rejection and allowance of the claims are respectfully requested.

Respectfully submitted,

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